Data Analysis and Interpretation

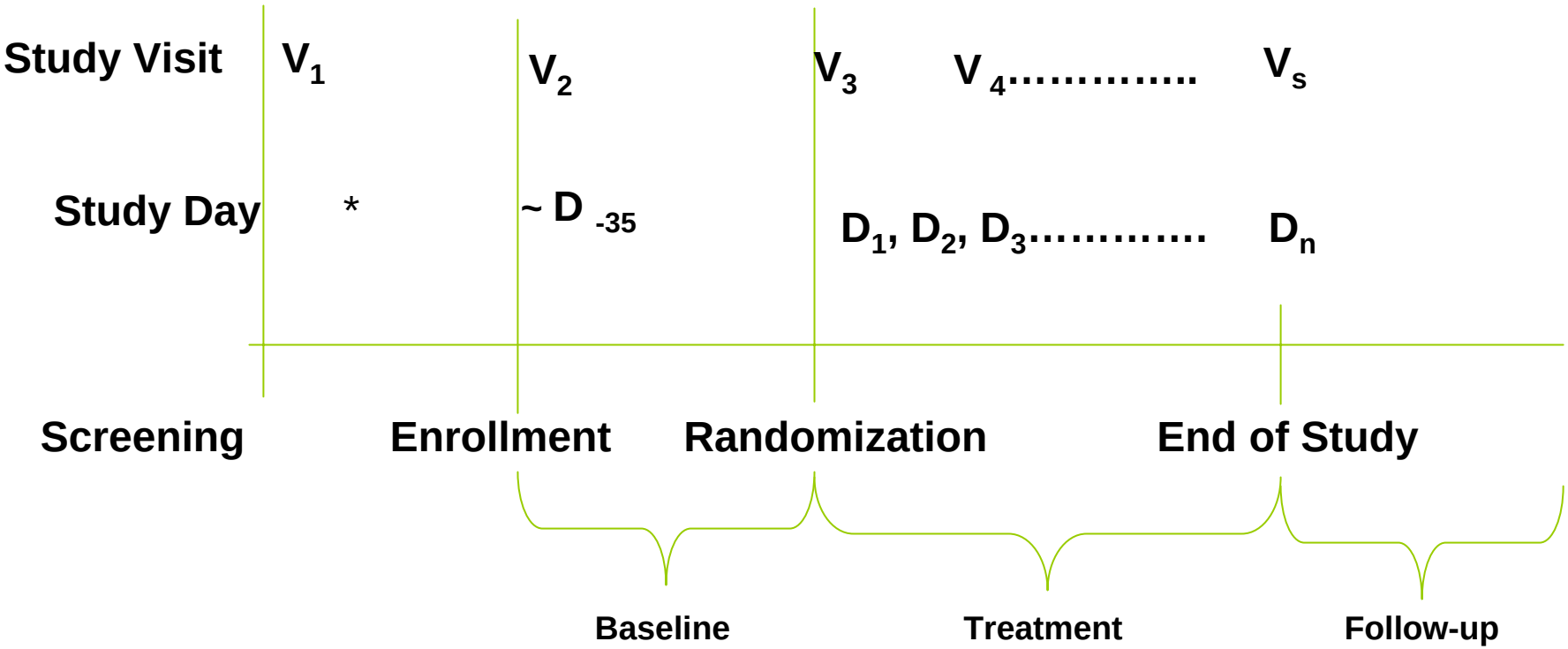
Charlie Cao

Takeda Global Research & Development Center, USA

Outline

- **Data Collection**
- **Data Derivation**
- **Data Analysis**
- **Data Interpretation**
- **Summary**

Data Collection - Schematic

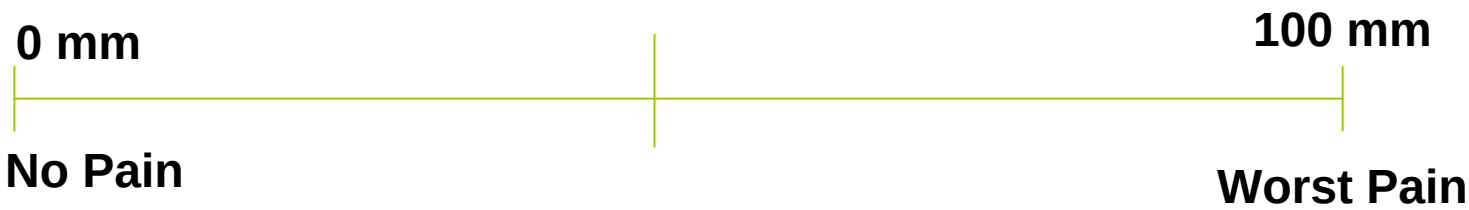


Data Collection ← Tools

- **B&B (Biberoglu & Behrman Scale)**
  - **0=none, 1=mild, 2=moderate, 3=severe.**
  - **Each scale is described by clinical symptoms or impairment of activity.**

- **BPI (Brief Pain Inventory)**
  - **0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10.**

- **VAS (Visual Analog Scale)**



Data Collection ← When/How

- **Daily, Weekly or Monthly**
- **Record pain score, not the change/improvement from baseline/previous visit**
- **Daily/weekly assessment is recommended if a quick onset of action is to be explored.**

Data Collection ← Electronic Diaries

- **Improve data quality by eliminating illegible and out of range responses**
- **Prevent back- and forward-filling of diary entries**
- **Enable more sensitive tools to reduce varibility and study size.**

Data Derivation ← Baseline (Daily/Weekly Assessment)

- **Baseline is the average of available observed daily/weekly values between enrollment and randomization visit for each primary endpoint.**

- **Time interval between enrollment and randomization visit should be at least one full menstrual cycle (e.g., 28~35 days) to ensure capture of dysmenorrhea and bleeding data.**

- **Any analgesic usage should be collected.**

Data Derivation ← Baseline (Monthly Assessment)

- **Baseline is the value prior to randomization based on monthly recall.**
- **Any analgesic usage whether supplied or not should be collected.**

Data Derivation ← final Visit (Daily/Weekly Assessment)

- **Average daily/weekly pain score for each primary endpoint within a full menstrual cycle is used. Pelvic pain and dysmenorrhea are mutually exclusive on the same day.**

- **If there is no bleeding during a reasonable time interval (eg 40 days, or one week plus the full cycle from baseline), all data during the interval are used to assess pelvic pain. Dysmenorrhea score is zero for that interval.**

- **Dyspareunia score is only from days/weeks with intercourse or avoidance of intercourse pain.**

Data Derivation ← final Visit (Monthly Assessment)

- **Pain score for each primary endpoint will be from monthly recall.**

- **Pain score is skewed toward to the last few days of the month – this is a particular problem for placebo group with continuing menses/dysmenorrhea.**

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Data Analysis ← Primary Endpoint

- **Composite One**
  - **Pelvic Pain + Dysmenorrhea at 5% significance level**
- **Separate Ones (Recommended!)**
  - **Pelvic Pain at 5% significance level**
  - **Dysmenorrhea at 5% significance level**
  - **Both are positive**

Data Analysis ← Population

- **Full Analysis Set (FAS)**
  - **All randomized subjects who received at least one dose of double-blind study drug and had at least one post-baseline efficacy assessment**

- **Per Protocol Set (PP)**
  - **All subjects in the FAS excluding those identified as major protocol violators**

Data Analysis ← Drop-outs

- **Patient drop outs, particularly in placebo subjects.**
  - **One analysis with LOCF (Last Observation Carry Forward).**
  - **Another analysis with observed data only.**

Data Analysis ← Analgesics

- **Separately analyze pain data and analgesics**
  - **OK if analgesics on study drug <= on controlled arm.**
- **Composite pain and analgesic data.**
  - **Problems about how to combine them**
- **Analgesic usage is a factor in the model.**

Data Analysis ← Grouping of Analgesics

- **E.G. (4-POINT SCALE)**
  - **None**
  - **Mild (<=50% of maximum recommended daily dose of non-narcotic analgesics)**
  - **Moderate (>50% of maximum recommended daily dose of non-narcotic analgesics)**
  - **Strong (any narcotic analgesics)**

Data Analysis ← Model

- **Daily/Weekly Collection (Continuous)**
  - **Analysis of Covariance: Change from baseline= Treatment +Baseline**
  - **Analgesics = treatment**

- **Monthly Recall (Nonparametric)**
  - **Response rate (i.e., improved or not)**
    - **Chi-square test without other factors**
    - **Cochran-Mantel-Haenszel (CMH) test using analgesics as a factor**

Data Interpretation (I)

- **Pain data and analgesic usage should be reviewed together.**
- **It is hard to interpret the results if study drug uses more analgesics and larger effect than placebo, but no adjustment of analgesics in the model.**
- **Placebo study may not be double-blinded if study drug has some obvious (adverse) events (e.g. hot flushes, absence of menses!).**

Data Interpretation (II)

- **Primary efficacy results from FAS and PP should be in the same direction.**

- **Secondly efficacy results such as global assessment, different pain tool (B&B) assessment should trend to the same direction as primary ones.**

Summary

- **Pelvic pain and dysmenorrhea are two co-primary endpoints while dyspareunia is a secondly endpoint.**

- **Daily pain assessment should be done if a quick onset of action is explored. It can also capture bleeding data and analgesic use more accurately. Electronic capture is helpful.**

- **Analysis of covariate with treatment as factor and baseline as a covariate is recommended for daily/weekly assessment.**

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